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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,444	05/02/2007	Parveen Kumar	RL-445US	1872
26815	7590	05/20/2008		
RANBAXY INC. 600 COLLEGE ROAD EAST SUITE 2100 PRINCETON, NJ 08540			EXAMINER	
			AFREMOVA, VERA	
			ART UNIT	PAPER NUMBER
			1657	
			MAIL DATE	DELIVERY MODE
			05/20/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/575,444

**Applicant(s)**

KUMAR ET AL.

**Examiner**

Vera Afremova

**Art Unit**

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 18-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/ISD)
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date 5/07/2007

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election of the group II, claims 2-17, in the reply filed on 2/20/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1 and 18-20 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions(s), there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 2/20/2008.

Claims 2-17 are under examination in the instant office action.

### ***Information Disclosure Statement***

The copy of the reference C2 was not provided and its citation lacks identification of pages to be considered.

### ***Specification***

The disclosure is objected to because of the following informalities:

The current address of the depository collection MTCC in India has to be present in the disclosure and updated, for example: on page 3, lines 22-25. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

#### ***Deposit***

Claims 2-19 are rejected under 35 U.S.C. 112, *first paragraph*, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

All claims require one of ordinary skill in the art to have access to a specific strain *Streptomyces glaucescens* MTCC 5115. Because the microorganism is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by the deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not clear from the specification or record that the microorganism is readily available to the public.

The objection and accompanying rejection may be overcome by establishing that each microorganism identified is readily available to the public and will continue to be so for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer, or by an acceptable deposit as set forth herein. See 37 CFR 1.801-1.809.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or a statement by an attorney of record over his/her signature and registration number, stating that the deposit has been made under the Budapest Treaty and that all restrictions imposed by the depositor on availability to the public of the deposited material will be irrevocably removed upon issuance of the patent would satisfy the deposit requirement. See 37 CFR 1.808.

Because MTCC has acquired the status of an International Depository in accordance to the Budapest Treaty, a declaration stating that all restrictions will be irrevocably removed upon issuance of the patent will overcome this rejection.

***Indefinite***

Claims 2-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites “using isolated *Streptomyces glaucescens* MTCC 5115” for producing tacrolimus, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 2 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 3 is rendered indefinite by recitation of a mutant of the strain MTCC 5115 because its characteristics are not defined in the as-filed specification.

Claim 6 is indefinite or contains typing error with regard to utilization of xylose, arabinose and salicin in the medium during fermentation because strain MTCC 5115 does not utilize these carbon sources as disclosed (table 3 page 6).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,194,378 (Salituro et al).

Claims are directed to a process for producing tacrolimus FK-506 wherein the process comprises culturing a strain of *Streptomyces glaucescens* MTCC 5115 or mutant thereof under submerged aerobic fermentation conditions in an aqueous nutrient medium; and isolating the tacrolimus from said medium. Some claims are further drawn to the use of the nutrient medium comprising a carbon source selected from glucose, galactose, glycerol, dextrose, starch, dextrin, maltose, etc.; a nitrogen source selected from yeast extract, soybean meal, cottonseed meal, corn steep liquor, wheat germ, etc.; and mineral salts selected from calcium, magnesium, sodium, cobalt, copper and potassium. Some claims are further drawn to incorporation of a defoaming agent into the nutrient medium. Some claims are further drawn to the use of temperature from about 20°C to about 40°C in the process; to the use of pH of about 6-8 during fermentation. Some claims are further drawn to the isolation of the tacrolimus by means of filtration, centrifugation, concentration, concentration under reduced pressure, lyophilization, extraction with a suitable solvent, treatment with adsorbents, treatment with resins, purification, crystallization and recrystallization.

The cited patent US 5,194,378 (Salituro et al) discloses a process for producing FK-506 (same as tacrolimus) wherein the process comprises culturing a representative of the *Streptomyces sp.* under submerged aerobic fermentation conditions in an aqueous nutrient medium and isolating the tacrolimus (see entire document including abstract). The fermentation medium comprises a carbon source selected from glucose, galactose, glycerol, dextrose, starch,

dextrin, maltose, etc. (col. 5, lines 39-45); a nitrogen source selected from yeast extract, soybean meal, cottonseed meal, corn steep liquor, wheat germ, etc. (col.5 , lines 45-55) and mineral salts selected from calcium, magnesium, sodium, cobalt, copper and potassium (col. 5, lines 60-65). The reference teaches incorporation of a defoaming agent into the nutrient medium (col.5, line 67); the use of temperature from about 20°C to about 40°C (col.6, lines 33); the use of pH of about 7 during fermentation (col. 6, line 38). The tacrolimus is recovered by conventional means of filtration, centrifugation, concentration, concentration under reduced pressure, lyophilization, extraction with a suitable solvent, treatment with adsorbents, treatment with resins, purification, crystallization and recrystallization (col. 7, lines 25-43).

Thus, the cited patent US 5,194,378 (Salituro et al) discloses a process for producing FK-506 by the same protocol as presently claimed. The producer strain in the cited method is different from the strain used in the claimed invention. However, the cited patent teaches that various representatives of *Streptomyces sp.* have been known and used for producing immunosuppressant compound FK-506 (col. 3, lines 45-55).

Thus, the use of various tacrolimus producing strains is considered to be substitution of equivalents. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use any and all available various tacrolimus producing strains with a reasonable expectation of success in recovering tacrolimus because protocols of culturing tacrolimus producing strains and recovering tacrolimus from fermentation cultures have been known in the prior art as adequately demonstrated by US 5,194,378 (Salituro et al). Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1657

May 16, 2008

VERA AFREMOVA

PRIMARY EXAMINER

/Vera Afremova/  
Primary Examiner, Art Unit 1657